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International Bureau

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| (51) International Patent Classification ⁷ : C12N 15/12, C07K 14/47, 16/18, G01N 33/566, C12Q 1/68, C12N 15/11, 15/62, A01K 67/027, A61K 38/00 | | A2 | (11) International Publication Number: WO 00/58473 (43) International Publication Date: 5 October 2000 (05.10.00) |
| (21) International Application Number: PCT/US00/08621 (22) International Filing Date: 31 March 2000 (31.03.00) (30) Priority Data: 60/127,607 31 March 1999 (31.03.99) US 60/127,636 2 April 1999 (02.04.99) US 60/127,728 5 April 1999 (05.04.99) US 09/540,763 30 March 2000 (30.03.00) US (63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Applications US 60/127,607 (CIP) Filed on 31 March 1999 (31.03.99) US 60/127,636 (CIP) Filed on 2 April 1999 (02.04.99) US 60/127,728 (CIP) Filed on 5 April 1999 (05.04.99) US 09/540,763 (CIP) Filed on 30 March 2000 (30.03.00) (71) Applicant (for all designated States except US): CURAGEN CORPORATION [US/US]; 555 Long Wharf Drive, 11th Floor, New Haven, CT 06511 (US). | | (72) Inventors; and (75) Inventors/Applicants (for US only): SHIMKETS, Richard, A. [US/US]; 191 Leete Street, West Haven, CT 06516 (US). LEACH, Martin [GB/US]; 884 School Street, Webster, MA 01570 (US). (74) Agent: ELRIFI, Ivor, R.; Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., One Financial Center, Boston, MA 02111 (US). (81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>Without international search report and to be republished upon receipt of that report.</i> | |
| (54) Title: NUCLEIC ACIDS INCLUDING OPEN READING FRAMES ENCODING POLYPEPTIDES; "ORFX" | | | |
| (57) Abstract The present invention provides open reading frames ORFX, encoding isolated polypeptides, as well as polynucleotides encoding ORFX and antibodies that immunospecifically bind to ORFX or any derivative, variant, mutant, or fragment of the ORFX polypeptides, polynucleotides or antibodies. The invention additionally provides methods in which the ORFX polypeptide, polynucleotide and antibody are used in detection and treatment of a broad range of pathological states, as well as to other uses. | | | |

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| | | | | |
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What is claimed is:

1. An isolated nucleic acid molecule encoding a polypeptide comprising an amino acid sequence that is at least 85% identical to a polypeptide including an amino acid sequence selected from the group consisting of SEQ ID NO:2*n*, wherein *n* is any integer 1-3161, or the complement thereof.
2. The isolated nucleic acid molecule of claim 1, said molecule hybridizing under stringent conditions to a nucleic acid sequence complementary to a nucleic acid molecule comprising the sequence of nucleotides selected from the group consisting of SEQ ID NO:2*n*, wherein *n* is any integer 1-3161, or the complement thereof.
3. The isolated nucleic acid molecule of claim 1, said molecule encoding a polypeptide comprising the amino acid sequence selected from the group consisting of SEQ ID NO: 2*n*, wherein *n* is any integer 1-3161, or an amino acid sequence comprising one or more conservative substitutions in the amino acid sequence selected from the group consisting of SEQ ID NO: 2*n*.
4. The isolated nucleic acid molecule of claim 1, wherein said molecule encodes a polypeptide comprising the amino acid sequence selected from the group consisting of SEQ ID NO: 2*n*, wherein *n* is any integer 1-3161.
5. The isolated nucleic acid molecule of claim 1, wherein said molecule comprises the sequence of nucleotides selected from the group consisting of SEQ ID NO:2*n*-1, wherein *n* is any integer 1-3161, or the complement thereof.
6. An oligonucleotide less than 100 nucleotides in length and comprising at least 10 contiguous nucleotides selected from the group consisting of SEQ ID NO:2*n*-1, wherein *n* is any integer 1-3161, or the complement thereof.
7. A vector comprising the nucleic acid molecule of claim 1.

compound, and detecting said complex, if present, thereby identifying said polypeptide in said sample.

17. A method of detecting the presence of a nucleic acid molecule of claim 1 in a sample, the method comprising contacting the sample with a nucleic acid probe or primer that selectively binds to the nucleic acid molecule and determining whether the nucleic acid probe or primer bound to the nucleic acid molecule of claim 1 is present in the sample.

18. A method for modulating the activity of the polypeptide of claim 10, the method comprising contacting a cell sample comprising the polypeptide of claim 10 with a compound that binds to said polypeptide in an amount sufficient to modulate the activity of the polypeptide.

19. The use of a therapeutic in the manufacture of a medicament for treating a syndrome associated with a ORFX-associated disorder, wherein said therapeutic is selected from the group consisting of:

- a) the nucleic acid of claim 1;
- b) the polypeptide of claim 10; and
- c) the antibody of claim 12.

20. A method for screening for a modulator of activity or of latency or predisposition to an ORFX-associated disorder, said method comprising:

- a) contacting a test compound with the polypeptide of claim 10; and
- b) determining if said test compound binds to said polypeptide,

wherein binding of said test compound to said polypeptide indicates the test compound is a modulator of activity or of latency or predisposition to an ORFX-associated disorder.

21. A method for screening for a modulator of activity or of latency or predisposition to an ORFX-associated disorder, said method comprising:

- a) administering a test compound to a test subject at an increased risk ORFX-associated disorder, wherein said test subject recombinantly expresses a polypeptide encoded by the nucleotide of claim 1;

wherein an alteration in the level of the nucleic acid in step (a) as compared to the control sample indicates the presence of or predisposition to said disease in said subject.

26. The method of claim 25, wherein said subject is a human.

27. A method of treating or preventing a pathological condition associated with an ORFX-associated disorder in a subject, the method comprising administering to said subject a polypeptide of claim 10 in an amount sufficient to alleviate or prevent said pathological condition.

28. The method of claim 27, wherein said subject is a human.

29. A method of treating or preventing a pathological condition associated with an ORFX-associated disorder in a subject, the method comprising administering to said subject a nucleic acid molecule of claim 1 in an amount sufficient to alleviate or prevent said pathological condition.

30. The method of claim 29, wherein said subject is a human.

31. A method of treating or preventing a pathological condition associated with an ORFX-associated disorder in a subject, the method comprising administering to said subject an antibody of claim 12 in an amount sufficient to alleviate or prevent said pathological condition.

32. The method of claim 31, wherein said subject is a human.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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International Bureau



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C07K 14/47, 16/18, G01N 33/566, C12Q 1/68, C12N
15/11, 15/62, A01K 67/027, A61K 38/00

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CT 06516 (US). LEACH, Martin [GB/US]; 884 School
Street, Webster, MA 01570 (US).

(21) International Application Number: PCT/US00/08621

(74) Agent: ELRIFI, Ivor, R.; Mintz, Levin, Cohn, Ferris,
Glovsky and Popeo, P.C., One Financial Center, Boston,
MA 02111 (US).

(22) International Filing Date: 31 March 2000 (31.03.2000)

(25) Filing Language: English

(81) Designated States (*national*): AE, AL, AM, AT, AU, AZ,
BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK,
DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
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UG, US, UZ, VN, YU, ZA, ZW.

(26) Publication Language: English

(30) Priority Data:
60/127,607 31 March 1999 (31.03.1999) US
60/127,636 2 April 1999 (02.04.1999) US
60/127,728 5 April 1999 (05.04.1999) US
09/540,763 30 March 2000 (30.03.2000) US

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent
(AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent
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MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM,
GA, GN, GW, ML, MR, NE, SN, TD, TG).

(63) Related by continuation (CON) or continuation-in-part
(CIP) to earlier applications:

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Filed on 31 March 1999 (31.03.1999)
US 60/127,636 (CIP)
Filed on 2 April 1999 (02.04.1999)
US 60/127,728 (CIP)
Filed on 5 April 1999 (05.04.1999)
US 09/540,763 (CIP)
Filed on 30 March 2000 (30.03.2000)

Published:

— With international search report.
— Before the expiration of the time limit for amending the
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(88) Date of publication of the international search report:
25 January 2001

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): SHIMKETS,

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: NUCLEIC ACIDS INCLUDING OPEN READING FRAMES ENCODING POLYPEPTIDES; "ORFX"

(57) Abstract: The present invention provides open reading frames encoding isolated polypeptides, as well as polynucleotides en-
coding ORFX and antibodies that immunospecifically bind to ORFX or any derivative, variant, mutant, or fragment of the ORFX
polypeptides, polynucleotides or antibodies. The invention additionally provides methods in which the ORFX polypeptide, polynu-
cleotide and antibody are used in detection and treatment of a broad range of pathological states, as well as to other uses.

WO 00/58473 A3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/08621

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| P,X | <p>M.D. ADAMS ET AL.: "The genome sequence of <i>Drosophila melanogaster</i>." SCIENCE, vol. 287, 24 March 2000 (2000-03-24), pages 2185-2195, XP002144875 the whole document</p> <p>-----</p> | 6 |

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claim : 1 to 32 partially

Isolated nucleic acid molecule encoding a polypeptide comprising an amino acid sequence that is at least 85% identical to a polypeptide including an amino acid sequence selected from a group consisting of SEQ ID NO 2n wherein n is 1, oligonucleotides less than 100 nucleotides in length and comprising at least 6 contiguous nucleotides from the above sequence, polypeptides encoded by said nucleotides, antibodies that bind to said polypeptide, pharmaceutical composition comprising said polypeptide and methods of detection, screening, therapeutic uses involving said polypeptide.

2. Claim : .

Inventions 2 to 3161

claims 1 to 32 partially :

Isolated nucleic acid molecule encoding a polypeptide comprising an amino acid sequence that is at least 85% identical to a polypeptide including an amino acid sequence selected from a group consisting of SEQ ID NO 2n wherein n is 2 to 3161, oligonucleotides less than 100 nucleotides in length and comprising at least 6 contiguous nucleotides from the above sequence, polypeptides encoded by said nucleotides, antibodies that bind to said polypeptide, pharmaceutical composition comprising said polypeptide and methods of detection, screening, therapeutic uses involving said polypeptide.